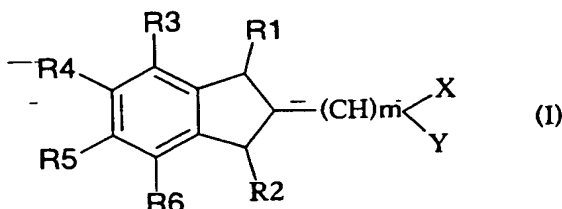


**EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY  
PREVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:**

1. A compound having structural formula (I):



stereoisomers thereof, or pharmaceutically acceptable salts or hydrates thereof,  
wherein:

**R1**, and **R2** are selected from the group comprising:

- (i) H
- (ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, or  $-(CH_2)_n$ -isoxazol, where  $n = 1, 2, 3, 4, 5$ , or 6;

**X** is an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol or isoxazol;

**Y** is a basic group selected from the group comprising 1° amino, 2° amino, 3° amino, quaternary ammonium salts, aliphatic 1° amino, aliphatic 2° amino, aliphatic

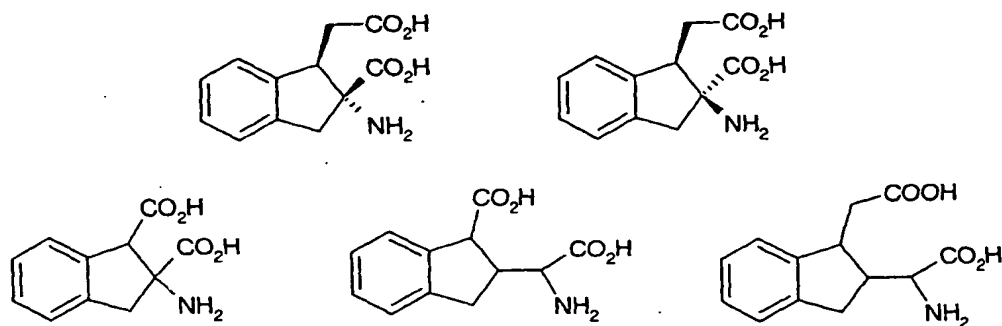
3° amino, aliphatic quaternary ammonium salts, aromatic 1° amino, aromatic 2° amino, aromatic 3° amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea or thiourea;

m is 0, 1;

R3, R4, R5, R6 are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or an acceptable ester thereof;

with the proviso that when X is COOH and Y is NH<sub>2</sub>, then at least one of R1 and R2 is other than H.

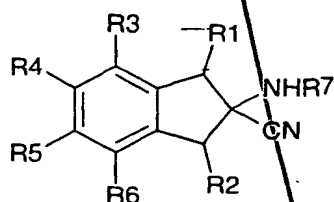
2. The compound according to claim 1, wherein R1 is H, CO<sub>2</sub>H or CH<sub>2</sub>CO<sub>2</sub>H.
3. The compound according to claim 1, wherein R2 is H, CO<sub>2</sub>H or CH<sub>2</sub>CO<sub>2</sub>H.
4. The compound according to claim 1, wherein said compound is selected from the group of compounds comprising:



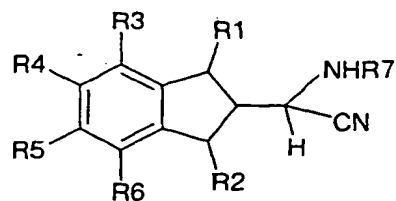
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1A1
5. A process for the preparation of a compound of Formula I, according to claim 1, or a pharmaceutically acceptable metabolically-labile ester or amide thereof, or a

pharmaceutically acceptable salts or hydrates thereof, which comprises:

- a) hydrolyzing a compound of formula (IIa) or (IIb):



(IIa)



(IIb)

wherein: **R1**, and **R2** are selected from the group comprising:

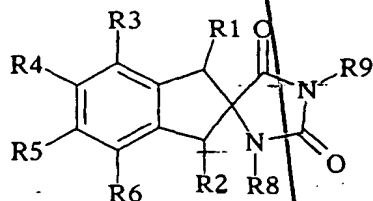
- (iii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, or  $-(CH_2)_n$ -isoxazol, where  $n = 1, 2, 3, 4, 5$ , or 6;

with the proviso that at least one of  $R_1$  and  $R_2$  is other than  $H$ ;

**R3, R4, R5, R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or an acceptable ester thereof; **R7** is a hydrogen atom or an acyl group. Preferred functional groups for **R7** are hydrogen and (C<sub>2</sub>-C<sub>6</sub>) alkanoyl group; or

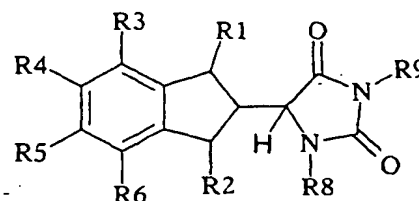
Q1 cont b)

hydrolyzing a compound of formula (IIIa) or (IIIb):



(IIIa)

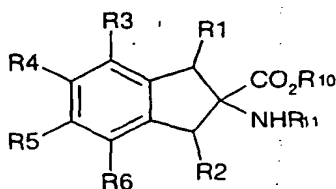
or



(IIIb)

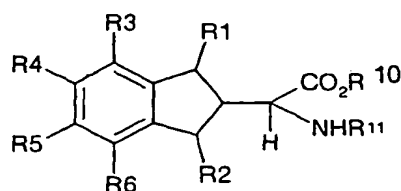
wherein: **R1**, **R2**, **R3**, **R4**, **R5** and **R6** are as defined above, **R8** and **R9** are each independently represent a hydrogen atom, a (C<sub>2</sub>-C<sub>6</sub>) alkanoyl group, a (C<sub>1</sub>-C<sub>4</sub>) alkyl group, a (C<sub>3</sub>-C<sub>4</sub>) alkenyl group or a phenyl (C<sub>1</sub>-C<sub>4</sub>) alkyl group wherein the phenyl is unsubstituted or substituted by halogen, (C<sub>1</sub>-C<sub>4</sub>) alkyl or (C<sub>1</sub>-C<sub>4</sub>) alkoxy, or a salt thereof, or

c) deprotecting a compound of formula (IVa) or (IV b):



(IVa)

or



(IVb)

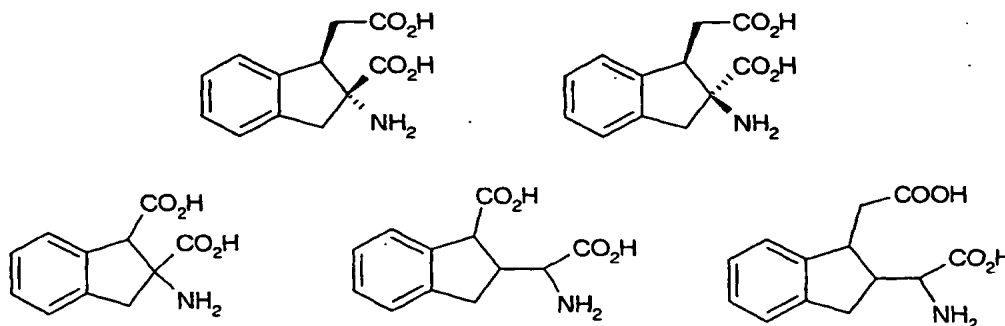
wherein: **R1**, **R2**, **R3**, **R4**, **R5** and **R6** are as defined above and **R10** is a hydrogen atom or a carboxyl protecting group, or a salt thereof, and **R11** represents a hydrogen atom or a nitrogen protecting group;

A<sup>1</sup> cont.

whereafter, if necessary and/or desired, the following steps are carried out:

- i) resolving the compound of Formula I;
- ii) converting the compound of Formula I into a non-toxic metabolically labile ester or amide thereof and/or
- iii) converting the compound of Formula I or a non-toxic metabolically labile ester or amide thereof into a pharmaceutically acceptable salt thereof.

6. A pharmaceutical formulation, which comprises a compound according to claim 1 and a pharmaceutically acceptable carrier, diluent or excipient.
7. The pharmaceutical composition according to claim 6, wherein said compound is selected from the group of compounds comprising:



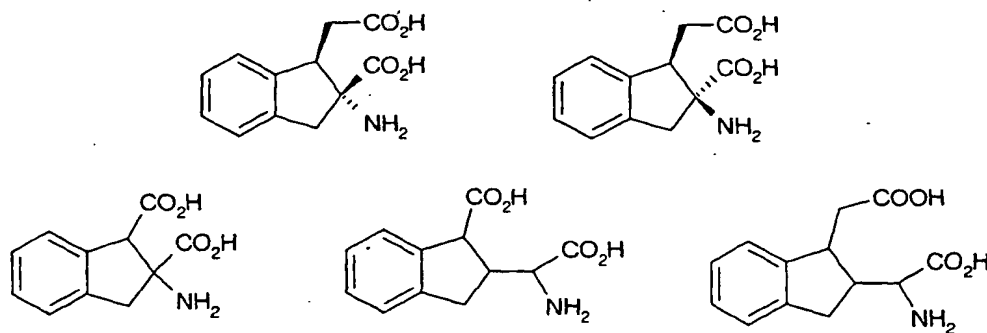
8. The use of the compound of structural formula (I) according to claim 1, in modulating one or more metabotropic glutamate receptor functions in warm blooded mammals, wherein said use comprises administering an effective amount of a compound of formula (I).

9. The use of the compound of structural formula (I) according to claim 1, in treating a

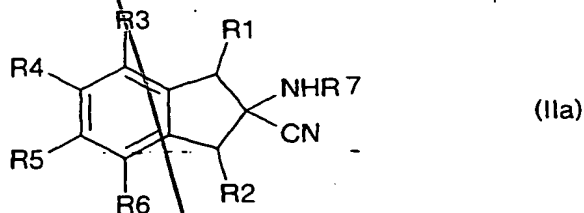
Q2 cont.

neurological disease or disorder selected from the group comprising: cerebral deficits subsequent to cardiac bypass surgery and grafting, cerebral ischemia, stroke cardiac arrest, spinal cord trauma, head trauma, perinatal hypoxia, hypoglycemic neuronal damage, Alzheimer's disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, ocular damage, retinopathy, cognitive disorders, idiopathic and drug-induced Parkinson's disease, muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance, withdrawal, and cessation (i.e. opiates, benzodiazepines, nicotine, cocaine, or ethanol), smoking cessation, anxiety and related disorders (e.g. panic attack), emesis, brain edema, chronic pain, sleep disorders, Tourette's syndrome, attention deficit disorder, and tardive dyskinesia, wherein said use comprises administering an effective amount of a compound of formula (I)

10. The use of the compound of structural formula (I) according to claim 1, in treating a psychiatric disease or disorder selected from the group comprising: schizophrenia, anxiety and related disorders (e.g. panic attack), depression, bipolar disorders, psychosis, and obsessive compulsive disorders, wherein said use comprises administering an effective amount of a compound of formula (I).
11. The use according to any one of claims 8, 9 and 10 wherein said compound is selected from the group of compounds comprising:



12. A compound of formula (IIa):



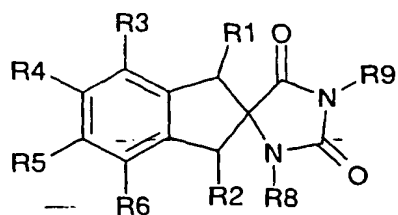
wherein: **R1**, and **R2** can each separately be selected from the group consisting of:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfinio, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfinio,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, or  $-(CH_2)_n$ -isoxazol, where  $n = 1, 2, 3, 4, 5$ , or 6;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof, **R7** is a hydrogen atom or an acyl group. Preferred functional groups for **R7** are hydrogen and  $(C_2-C_6)$  alkanoyl groups;

with the proviso that at least one of **R1** and **R2** is other than H.

13. A compound of formula (IIIa):



(IIIa)

wherein: **R1**, and **R2** can each separately be selected from the group consisting of:

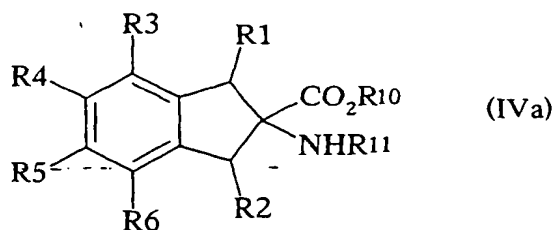
- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfinio, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfinio,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, or  $-(CH_2)_n$ -isoxazol, wherein  $n = 1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R8** and **R9** are each independently represent a hydrogen atom, a  $(C_2-C_6)$  alkanoyl group, a  $(C_1-C_4)$  alkyl group, a  $(C_3-C_4)$  alkenyl group or a phenyl  $(C_1-C_4)$  alkyl group wherein the phenyl is unsubstituted or substituted by halogen,  $(C_1-C_4)$  alkyl or  $(C_1-C_4)$  alkoxy, or a salt thereof;

with the proviso that at least one of **R1** and **R2** is other than H.



14. A compound of formula (IVa):



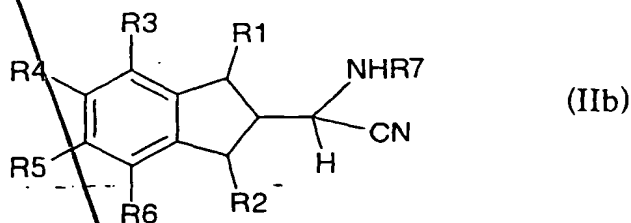
wherein: **R1**, and **R2** can each separately be selected from the group consisting of:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, or  $-(CH_2)_n$ -isoxazol, wherein  $n = 1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R10** is a hydrogen atom or a carboxyl protecting group, or a salt thereof, and **R11** is a hydrogen atom or a nitrogen protecting group;

with the proviso that at least one of **R1** and **R2** is other than H.

15. A compound of formula (IIb):



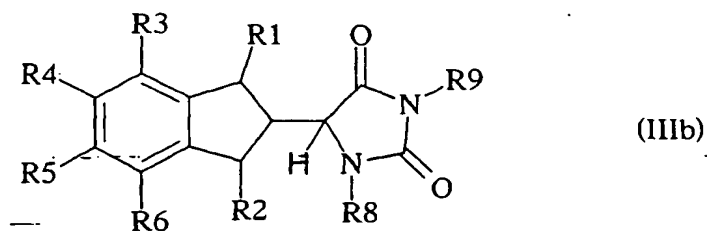
wherein: **R1**, and **R2** can each separately be selected from the group consisting of:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, or  $-(CH_2)_n$ -isoxazol, wherein  $n = 1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R7** is a hydrogen atom or an acyl group. Preferred functional groups for **R7** are hydrogen and  $(C_2-C_6)$  alkanoyl groups;

with the proviso that at least one of **R1** and **R2** is other than H.

16. A compound of formula (IIIb):



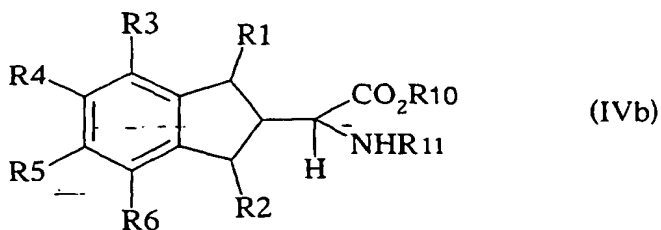
wherein: R1, and R2 can each separately be selected from the group consisting of:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, or  $-(CH_2)_n$ -isoxazol, wherein  $n = 1, 2, 3, 4, 5$ , or  $6$ ;

R3, R4, R5 and R6 are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; R8 and R9 are each independently represent a hydrogen atom, a  $(C_2-C_6)$  alkanoyl group, a  $(C_1-C_4)$  alkyl group, a  $(C_3-C_6)$  alkenyl group or a phenyl  $(C_1-C_4)$  alkyl group wherein the phenyl is unsubstituted or substituted by halogen,  $(C_1-C_4)$  alkyl or  $(C_1-C_4)$  alkoxy, or a salt thereof;

with the proviso that at least one of R1 and R2 is other than H.

17. A compound of formula (IVb):



wherein: **R1**, and **R2** can each separately be selected from the group consisting of:

- i) H
- ii) an acidic group selected from the group comprising carboxy, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol,  $-(CH_2)_n$ -carboxy,  $-(CH_2)_n$ -phosphono,  $-(CH_2)_n$ -phosphino,  $-(CH_2)_n$ -sulfono,  $-(CH_2)_n$ -sulfino,  $-(CH_2)_n$ -borono,  $-(CH_2)_n$ -tetrazol, or  $-(CH_2)_n$ -isoxazol, wherein  $n = 1, 2, 3, 4, 5$ , or  $6$ ;

**R3**, **R4**, **R5** and **R6** are independently H, nitro, amino, halogen, tritium, trifluoromethyl, trifluoroacetyl, sulfo, carboxy, carbamoyl, sulfamoyl, or pharmaceutically acceptable ester or salt thereof; **R10** is a hydrogen atom or a carboxyl protecting group or a salt thereof, and **R11** is a hydrogen atom or a nitrogen protecting;

with the proviso that at least one of **R1** and **R2** is other than H.